U.S. Military Fatalities due to Neisseria meningitidis: Case Reports and Historical Perspective

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U.S. Military Fatalities due to *Neisseria meningitidis*: Case Reports and Historical Perspective

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ABSTRACT Meningococcal disease has historically been associated with military populations, particularly during periods of mobilization. Although the U.S. military has now been engaged in conflicts for nearly a decade, the incidence of meningococcal disease in the U.S. population as a whole has reached historic lows. Despite vaccination of all service members in basic military training, the risk of meningococcal disease appears to be equal to or greater than that of the civilian population. These 3 case reports of recent fatalities in the U.S. military and their historic contexts illustrate the circumstances under which meningococcus can strike and highlight the need for continued vigilance in military populations.

INTRODUCTION

From the earliest days of its recognition as a distinct entity, cerebrospinal meningitis has been known to pose a particular threat to military populations. In a summary of 38 epidemics that occurred in garrisons across France, Casimir Broussais of the military hospital at Val-de-Grâce in 1845 suggested that this disease affects military populations with "une sorte de prédilection."[1] Residents of a mining town in Pennsylvania in the midst of an epidemic in 1864 made the same association and sought to protect themselves by burning down buildings that had served as military barracks.[2] Even after large epidemics among civilian populations in the 1880s and 1890s, Jaeger referred to meningococcal disease as a soldier's disease "par excellence."[3] Now, with the U.S. military extended in 2 theaters of conflict, the incidence of meningococcal disease in the United States has decreased to historic lows.[4] To reassess the risks posed by the meningococcus to military populations, we have acquired medical records from 3 of the most recent fatalities in the U.S. military. These cases demonstrate the ongoing need for vigilance of meningococcal disease in military populations.

NEW RECRUITS

Case 1

A 19-year-old male soldier, 3 weeks into his Advanced Individual Training, presented to Sick Call at a tertiary Military Treatment Facility at 6 a.m. with a chief complaint of fever, headache, and vomiting. He had had fatigue and myalgias for about 3 days, but attributed these to his military training. He had a temperature of 103°F, heart rate of 120, and blood pressure of 122/67. Oropharynx, lungs, and skin were normal on examination. The initial white blood cell (WBC) count was $2.0\times10^3/mm^3$ with 88% neutrophils, and his platelets were just below normal at $147\times10^3/mm^3$. He was treated symptomatically with acetaminophen, ketorolac, and promethazine, but his temperature remained above 102°F. He was admitted to the Military Treatment Facility and started on ceftriaxone, vancomycin, doxycycline, and dexamethasone at 1 p.m. Blood tests on admission showed a WBC count of 1.8 and a platelet count of 33. Intracellular diplococci were seen on his peripheral blood smear. His prothrombin time (PT) and partial thromboplastin time (PTT) were prolonged to 31 seconds and 92 seconds, respectively. By 3 p.m., he was in respiratory distress and was hypotensive, with a progressive purpuric rash, prompting intubation and transfer to the intensive care unit (ICU). Despite the use of pressors, his condition deteriorated rapidly and he expired at 3 a.m.

Gram-variable cocci were detected in blood cultures later that morning, which were subsequently identified as *Neisseria meningitidis* group C.

Historic Background

The basic military training environment has long been recognized as a period of particular risk for meningococcal disease. For many new recruits, particularly in the first half of the last century, basic training represents the first time they come in close contact with individuals from other geographical areas. Under such circumstances, virulent strains of meningococci are passed to individuals without prior exposure, leading to clinical cases and, particularly in the absence of effective chemoprophylaxis for close contacts, epidemics.[5] In addition to exposure factors, the extreme physical exertion of those not yet fully conditioned to the rigors of military training has been presumed to further predispose recruits to disease.[6]

The most dramatic evidence of the association between basic training and meningococcal disease comes from the First World War. Meningococcal disease had been occurring among civilian populations in Europe since the 1880s and in

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the United States since the turn of the century.[3] Coincident with their period of rapid military expansion, the militaries of France[7] and England[8] experienced dramatic increases in the incidence of meningococcal disease in 1915. In the U.S. Army, a similar increase in disease rate did not occur until troops mobilized for war 2 years later.[6] Epidemics were particularly severe in camps training soldiers from rural areas (Camp Jackson, South Carolina; Camp Beauregard, Louisiana; and Camp Funston, Kansas), but cases occurred across the country in 37 of 39 camps training new recruits.[6] Recommendations for soldiers to sleep head to foot and other distancing measures that are still in use today[9] were implemented at this time.[10]

U.S. involvement in the Second World War also led to a dramatic increase in cases. Toward the end of the war, universal prophylaxis of new recruits with sulfa antibiotics was implemented.[11] The incidence of disease among new recruits dropped significantly and remained low through the period of the Korean War.[12]

In the early 1960s, the predominant serogroup causing disease in the United States switched from A to B, accompanied by an increase in antibiotic resistance.[13] The problem of meningococcal epidemics in basic training centers recurred and continued despite sulfa prophylaxis of the entire garrison at Fort Ord, California.[14] This proved to be the impetus that would lead the Army to develop a capsular polysaccharide vaccine.[15] Although the group B capsule was discovered to be poorly immunogenic,[16] from 1962 to 1968, the predominant serogroup switched to C. Universal vaccination of new recruits with group C polysaccharide was implemented in 1971, with a dramatic drop in cases.[17]

MOBILIZATION TRAINING

Case 2

A 26-year-old male Army noncommissioned officer, already a combat veteran, was assigned as an individual augmentee to an Army National Guard unit mobilizing for deployment to Iraq. After 3 weeks into training, he presented to the Troop Medical Clinic at 9 a.m. with sudden onset of fever, shaking chills, generalized myalgias, cough, vomiting, and watery diarrhea. His temperature was 105.8°F. Because of the high temperature, he was transferred to a civilian clinic for further evaluation, where his temperature was recorded as 99.0°F. His WBC count was 3.5, and despite a pulse of 118 beats per minute, he was discharged with a diagnosis of possible viral syndrome.

He returned to the Troop Medical Clinic at about 2 p.m. with worsening symptoms, a systolic blood pressure of 90/40 mmHg, temperature of 103.3°F, and heart rate of 100. He was given 60mg of ketorolac intramuscularly and transferred to a civilian hospital, where he was admitted to the ICU at 4:30 p.m. Multiple ecchymotic and purpuric spots and conjunctival petechiae were noted, and these progressed rapidly. WBC count on admission was 2.9 (40% segs and 32% bands), and neutrophils showed toxic granulation with Dohle bodies and vacuoles. His platelet count was 98, PT 22.3, PTT 58.9, and creatinine 2.2 mg/dL. He was started on levofloxacin, ceftriaxone, and doxycycline. A central line and endotracheal tube were placed. Repeat blood work at 8 p.m. showed a PT >120 and PTT >200, platelet count of 10, and creatinine 2.5. The patient was transferred to a tertiary care facility for dialysis but expired en route.

Blood cultures showed gram-negative diplococci at 14 hours, subsequently identified as *N. meningitidis* group B.

Historic Background

In previous wars, basic training was often followed immediately by mobilization to the combat theater, resulting in a continuous period of crowded living conditions and increased risk of meningococcal disease. In this context, the first microbiologically confirmed outbreak of meningococcal disease in the U.S. Army occurred en route to Cuba following the Spanish American War,[18] and a shipboard outbreak among Canadian recruits was blamed for starting the epidemic of cases in the British military in 1915.[8]

Predeployment training for the current conflicts is undergone by established units, of which recent recruits make up a relatively small percentage. The risk of meningococcal disease among seasoned troops under such circumstances may be more akin to the risk of cases among permanent garrison staff during the training center outbreaks of previous decades. During the Fort Ord outbreak of 1962–1964, 2 out of 189 active military cases occurred among regular garrison personnel.[14] At Fort Leonard Wood in 1970, only 1 out of the 53 military cases occurred in a member of the permanent party.[19]

The soldier in this report—though older and more experienced than many of those with whom he was training, as an individual augmentee to another state's National Guard unit—was the newcomer geographically, and presumably immunologically, speaking.

COMBAT THEATER

Case 3

A 37-year-old female Air Force noncommissioned officer presented to an aid station in Iraq at 3:20 p.m. with a chief complaint of nausea for 24 hours. She also complained of weakness, chills, and fever. She had been in theater for 2 months.

The patient was awake, alert, and oriented and did not appear in acute distress. The physical examination was unremarkable. Her temperature was 98.2°F, blood pressure 110/79, and heart rate 69. She was treated with acetaminophen and promethazine and discharged with instructions to stay well hydrated.

At 8:30 p.m., she returned with progressive weakness and 9/10 pain in her muscles. She had developed headache and abdominal discomfort. On examination she appeared weak and dehydrated, with a temperature of 98.3, blood pressure

of 67/38, heart rate of 120, and respiratory rate of 30. Her extremities were cold to the touch. She was administered 3L of normal saline over the next 4 hours, as well as ketorolac, ondansetron, and ranitidine, intravenously. She showed no signs of improvement and was evacuated to a Combat Support Hospital.

Upon transfer she was in respiratory distress, with conjunctival and axial petechiae and ecchymoses at tourniquet and blood draw sites. Temperature was 100.3°F, blood pressure 115/75, heart rate 104, respiratory rate 34, and pulse oximetry 85%. She was admitted to the ICU, intubated, and over subsequent hours, became edematous, unresponsive, and cyanotic. Her skin became diffusely purpuric. She was scheduled for evacuation to Landstuhl Regional Medical Center for dialysis but expired en route.

Blood cultures returned positive at 32 hours, subsequently identified as *N. meningitidis* group B.

Historic Background

Despite the large number of cases reported during basic training and mobilization, reports of meningococcal epidemics in combat theaters are relatively rare. This may be due to less time spent in confined barracks or to the higher level of herd immunity, where even the newest recruits have already been exposed, through basic training and perhaps an ocean crossing, to multiple meningococcal strains.

Over 100 cases were reported among Prussian troops deployed in France during the Franco–Prussian War in 1870–1871.[3] But, as of that time, cerebrospinal meningitis had only been reported sporadically in the Prussian army,[3,20] and no epidemics had occurred during recent campaigns in Denmark (Second Schleswig War, 1864) or Bohemia (Austro–Prussian War, 1866).[3] These troops simply may not have encountered meningococci before deploying to an area where it had become endemic. Among the French in World War I, despite the high incidence of disease in training camps and the conditions of crowding and poor hygiene that prevailed in the trenches, only a few isolated cases occurred on the front lines.[7] Among American troops in the two World Wars, the majority of cases in Europe occurred among newly arrived troops.[11] Meningococcal disease among troops in Korea[12] and Vietnam[21] was "not a feature" of those conflicts.

This case, unfortunately, is a reminder of the limited utility of recognizing such trends.

CURRENT THREAT OF MENINGOCOCCAL DISEASE TO THE U.S. MILITARY

All 3 of these patients succumbed to sepsis without developing distinct signs of meningitis. The initial presentation was nonspecific, with nausea and muscle aches being the most common accompaniments to fever. The diagnosis was not obvious on presentation for any of these cases, and the time from presentation to first dose of antibiotics ranged from 6 to 12 hours. It is evident from the reports that case 1 delayed presenting because he attributed his symptoms to military training, and that cases 2 and 3 were initially presumed to have the more common diagnoses of viral infection and dehydration, respectively. Cases 2 and 3 may have been adversely affected by the remoteness of their duty stations since both died while being transferred to higher levels of care, though by that point in their respective clinical courses, the prognosis was already grim.

These cases represent 3 of 4 meningococcal deaths in the U.S. military reported to the Naval Health Research Center (NHRC) for calendar years 2007–2008, with no fatalities reported for 2009–2010. The fourth fatality occurred at a service academy where the risk was perhaps defined more by residence in a college dormitory than by active military service. All 4 fatalities are summarized in Table I. For calendar years 2006–2008, 14 additional cases from the active military were reported to NHRC, either directly (n = 12) or by the Armed Forces Health Surveillance Center (AFHSC) through the Defense Medical Surveillance System. Of the 18 total cases, 6 were due to serogroup B, 4 to C, 4 to Y, and 4 unknown.

Among an active military population of about 1.41 million, 18 cases in 3 years represent an incidence of 0.427 cases per 100,000 per year, compared with 1.4 cases per 100,000 per year for the period 1983–1998.[17] To compare with the contemporary civilian U.S. population, data from the National Notifiable Diseases Surveillance System from 2006–2008, broken down by age cohorts (18–21, 22–30, 31–40, 41–50, and 51–59 years) and weighted in proportion to the representation of these cohorts in the active U.S. military (19.9%, 47%, 24.8%, 8%, and 0.6%, respectively), gives a corresponding incidence of 0.330 cases per 100,000 for 2006, 0.305 cases per 100,000 for 2007, and 0.279 cases per 100,000 for 2008, or 13.07 cases per 1.41 million per 3 years. Therefore, the incidence of meningococcal disease in the U.S. military appears to be higher than in the age-matched civilian U.S. population, but this difference is not statistically significant (P = 0.113

TABLE I. Summary of Meningococcal Fatalities in the U.S. Military, 2007–2009

	Age	Sex	Time Since Basic Military Training	Chief Complaint	Clinical Syndrome	Serogroup	Time From Symptom Onset to Presentation	Time From Presentation to Antibiotic Treatment
Case 1	19	Male	3 Weeks	Fever, Vomiting,	Sepsis	C	<6 Hours	~6 Hours
Case 2	26	Male	4 Years	Fever, Vomiting	Sepsis	B	<3 Hours	~11 Hours
Case 3	37	Female	>10 Years	Fever, Nausea, Weakness	Sepsis	B	~24 Hours	5–7 Hours
Academy Student	20	Male	4 Months	Fever, Headache	Sepsis	Y	~10 Hours	12 Hours

for 18 or more cases, Poisson distribution). It should be noted that the data collection systems for these 2 populations are not identical and may differ in accuracy or completeness.

Despite universal vaccination against groups A, C, Y, and W-135 upon entry into basic military training, 7 of 14 cases for which the serogroup is known appear to represent vaccine failures (3 group Y, 4 group C; up-to-date vaccination status confirmed in all 7 cases). Vaccines that target antigens other than the polysaccharide capsule are being developed to extend coverage to group B[22]; such vaccines might also provide additional protection against these capsular groups.

CONCLUSIONS

Despite the relatively high operational tempo over the period of analysis, meningococcal disease in the military has declined in incidence since 1998. All recruits in basic military training receive a tetravalent vaccine; however, the risk of meningococcal disease still appears to be equal to or greater in the military than in an age-matched civilian population. An ongoing vigilance for meningococcal disease should be maintained, particularly among new recruits and those who have recently changed units or duty locations. The circumstances of service and the physical and medical conditions commonly encountered in military populations may lead to delays in presentation, diagnosis, and timely access to advanced levels of care, all of which may adversely affect outcome.

Cases of meningococcal disease occurring in the U.S. Department of Defense should be reported to the Naval Health Research Center, Department of Respiratory Diseases Research, (619) 553-8515 or 553-8163; nhrc-mgc@med.navy.mil.

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14. ABSTRACT

In order to reassess the risks posed by meningococcal disease to military populations, we have acquired medical records of three of the most recent fatalities in the U.S. military and present the case studies. These cases represent three of four meningococcal deaths in the U.S. military reported to the Naval Health Research Center for calendar years 2007–2009. The fourth fatality occurred at a service academy where the risk was perhaps defined more by residence in a college dormitory than by active military. Among an active military population of about 1.43 million, 26 cases in 3 years represent an incidence of 0.606 cases per 100,000 per year, compared with 1.4 cases per 100,000 per year for the period 1983–1998. Meningococcal disease in the military has declined in incidence since 1998. All new recruits receive a tetravalent vaccine; however, the risk of meningococcal disease still appears to be greater in the military than in an age-matched civilian population.

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